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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/509,239	03/23/00	BRUCK	C B45110

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SMITHKLINE BEECHAM CORPORATION
CORPORATE INTELLECTUAL PROPERTY-US, UW22
P. O. BOX 1539
KING OF PRUSSIA PA 19406-0939

EXAMINER	
WINKLER,U	
ART UNIT	PAPER NUMBER
1648	13

DATE MAILED: 10/22/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/509,239	BRUCK ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-77* is/are pending in the application.

4a) Of the above claim(s) *55-77* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The Amendment filed 20 August 2001 (Paper No. 13) in response to the Office Action of 20 February 2001 is acknowledged and has been entered. Claims 32-77 are pending and claims 32-54 are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

The office acknowledges the amendment to the specification updating the status (pending, allowed, ect.) of all parent priority applications in the first line of the specification.

The newly submitted drawings of 20 August 2001 have been review by the Draftsperson and are objected to due to minor informalities please see attached review. Correction is required.

The objection of claim 32 for having informalities **is withdrawn** in view of applicant's amendment to the claim.

The rejection of claims 32-53 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention **is withdrawn** in view of applicants amendment deleting the term "vaccine" from the claims.

The rejection of claims 32, 36 and 50-54 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention **is maintained** for reasons of record. Applicant's argument that there is sufficient written description in the specification to identify the mutated Tat which possesses the requisite features for applicant's invention. It is noted that the features upon which applicant relies (i.e., biologically inactive) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims.

It is noted that the following rejection was duplicated in the prior office action; the examiner apologizes for the oversight. The rejection of claims 32, 35 and 50-54 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention **is withdrawn** in view of applicant's amendments that the composition now only need be "immunogenic" and therefore does not have to meet the rigorous efficacy requirement of a "vaccine".

The rejection of claims 32, 35, 36 and 50-54 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make

and/or use the invention **is withdrawn** in view of applicant's statement that the Nef, Tat and fusion protein orientation is not critical to the invention. This in combination with the amended to the claim that the composition only needs to meet the requirement of being immunogenic is sufficient to withdraw the rejection.

The rejection of claim 32 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is withdrawn** in view of applicant's amendments to the claims indicating that it requires an "immunogenic composition".

New rejections in view of applicant's amendments:

Claims 32-34, 37, 38 and 54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification does not provide a written description for "immunogenic derivative", nor does it provide a description of the structural and functional limitations that are considered to be an "immunogenic derivative". The instant claims now appear to recite limitations which were not clearly disclosed in the specification as filed and now change the scope of the instant disclosure. The limitation "immunogenic derivative" introduces a new concept and, therefore, does not meet the written description requirement.

Claims 32-34, 37, 38 and 54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The specification does not provide a clear definition of "an immunogenic derivative" and does not set forth the metes and bounds of the claim. There is insufficient information regarding the structural and functional constraints of the "immunogenic derivative".

Claims 32 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The specification does not provide a clear definition of "the derivative of the Tat protein is an immunogenic mutated Tat protein" and does not set forth the metes and bounds of the claim. There is insufficient information regarding the structural and functional constraints of the "derivative as an immunogenic mutated Tat protein". The confusion arises because it is not clear that the derivative, which presumably is only a portion of the Tat protein, actually must contain the mutation. The derivative can be obtained from an area of the protein that contains no mutation at all.

Claims 32 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The specification does not provide a clear definition of "the derivative of the Nef protein is an immunogenic mutated Nef protein" and does not set forth the meets and bounds of the claim. There is insufficient information regarding the structural and functional

constraints of the "derivative as an immunogenic mutated Nef protein". The confusion arises because it is not clear that the derivative, which presumably is only a portion of the Nef protein, actually must contain the mutation? The derivative can be obtained from an area of the protein that contains no mutation at all.

Claims 32, 33, 34, 36, 40-49 and 54 rejected under 35 U.S.C. 103(a) as being unpatentable over Schluesener (Journal of Neuroscience 1996, found on 892 of paper No. 4) and Hinkula et al. (Journal of Virology 1997), claim 35 further in view of Gaynor (U.S. Pat. No. 5,597,895), claims 50-53 further in view of Berman et al. (U.S. Pat No. 5,864,027) or claims 37-39 further in view of Forsgren (U.S. Pat. No. 5,888,517).

The instant invention is drawn to a composition comprising an HIV Tat and Nef fusion protein or a Tat – Nef fusion protein linked to another immunogenic protein, such as *H. influenza* lipoproteins. In addition, the immunogenic composition comprises HIV gp-160 or derivative thereof as well.

Schluesener teach a composition of a polyvalent Tat peptide as an immunogen. The reference teaches linking HIV Tat to three pathogenic T-cell epitopes, this fusion combination improves their immunogenicity. The reference does not teach immunizing with Nef as well.

Hinkula et al. teach a composition of Nef, Tat or Rev as an immunogen. The reference also teaches that due to the polymorphism found in the human population, an effective vaccine will require the combination of many proteins or glycoproteins (page 5538 last paragraph). The reference does not teach a Tat-Nef fusion protein.

Gaynor et al. teaches the composition of mutated Tat proteins (see claim 4). The reference does not teach combining the composition with Nef as an immunogen.

Berman et al. teach the composition comprising HIV env, gp120 fragments as immunogenic compositions. The reference does not teach combining the composition with Nef or Tat.

Forsgren teach *H. influenza* lipoprotein D fusion protein as an immunogenic composition (see claim 5). The reference does not teach coupling the lipoprotein to an HIV immunogen.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to formulate a polyvalent immunogen using multivalent linked HIV antigens (as taught by Schluesener) as well as multiple HIV antigens (as taught by Hinkula et al.) to confer or to increase immune responses, including to antigen Tat and antigen Nef. The ordinary artisan would have been motivated to provide many different peptides and proteins of the same pathogen in order to maximize the immune response against the pathogen. One of ordinary skill in the art at the time the invention was made would have been motivated to fuse the HIV Tat and Nef that is to be used as an immunogen following the teachings of Hinkula et al. which indicate that a successful vaccine/immunogen will require many proteins. It would also be obvious to the ordinary artisan that making a fusion protein containing many epitopes using a tag (such as histidine or GST) for purposes of purification which would simplify the production of the immunogen, the motivation being the simplified procedure. Optimizing the formulation of the composition (specifically claims 43- 49), including the addition of adjuvants or protein modification or denaturation agents fall within the skill of an ordinary artisan. If the addition of the modulating compounds produces an unexpected result, applicant needs to point out what the unexpected results are. The references of Gaynor et al, Berman et al. or Forsgren teach the additional limitations in view of the primary references Schluesener and Hinkula et al. It is

prima facie obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose in order to form a third composition that is to be used for very same purpose; the idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06. Therefore, the instant invention of claims 32, 33, 34, 40-49 and 54 are obvious over Schluesener and Hinkula et al. further in view of Gaynor or Berman et al. or Forsgren.

Conclusion

Claims 32-54 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ulrike Winkler, Ph.D.

JEFFREY STUCKER
PRIMARY EXAMINER